IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

FERREE

Serial No.: 10/787,469

Filed: February 26, 2004

For: ANNULUS FIBROSIS AUGMENTATION METHODS (as amended)

Group Art Unit: 3733

Examiner: David C. Comstock

DECLARATION OF BRET FERREE, M.D.

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Bret Ferree, M.D., do declare that:

1. I am a Board Certified Orthopedic surgeon specializing in spinal surgery. I am also a voluntary Assistant Professor at the University of Cincinnati. I received an M.D. from the University of Cincinnati College of Medicine (Cincinnati, Ohio) in 1986. I also completed a Spinal Surgery fellowship in the Department of Orthopedic Surgery at Tufts Medical School, New England Baptist Hospital (Boston, Massachusetts). In my capacity as an orthopedic surgeon specializing in spinal surgery, I have performed over 1,500 surgeries to repair disc herniations. I am the inventor of this application and President and Chief Executive Officer of Anova Corporation, assignee of the above-referenced application. I have a financial interest in this application.

2. I have reviewed U.S. Application Serial No. 10/787,469, the pending claims, and the office action dated September 20, 2007.

3. I have also reviewed the following references.

- Yuan et al., U.S. Patent No. 5,681,310 "Vertebral Auxiliary Fixation Device Having Holding Capability"
- Grooms et al., U.S. Patent No. 6,045,554 "Cortical Bone Interference Screw"
- Cauthern, U.S. Patent No. 6,592,625 "Spinal Disc Annulus Reconstruction Method And Spinal Disc Annulus Stent"

4. Both anterior spinal fixation and fusion require a bone graft or cage to be placed into the disc space. Implant surface area is known to have an important effect on rates of fusion. In levels of the spine that do not properly fuse, cage subsidence occurs and provides less than 30% interbody support. It has therefore been reported that, in order to optimize fusion, the surgeon should maximize surface area support of the intervertebral cage or bone graft. See McClellan et al., "Proceedings of the NASS 22nd Annual Meeting," *The Spine Journal* 7 (2007): 1S-163S (Exhibit 1).

5. Annulus fibrosis tissue is known to be thick and, if used in a three-segment implant as required by claim 15, would result in implanted annulus fibrosis tissue being placed "adjacent the diseased annulus fibrosis." Because of this arrangement, the thick annulus fibrosis tissue would significantly reduce the size of the cage or bone graft material that can be placed into the disc space. Thus, one skilled in the art, trying to maximize surface area support of the implant, would actually seek to avoid use of annulus fibrosis tissue as the second segment for purposes of spinal fusion and fixation.

6. I further declare that all statements made in this Declaration of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section

1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the patent and application involved in the present proceedings.

Dated: 12/17/07

Bret Ferree, M.D.

EXHIBIT 1

FDA DEVICE/DRUG STATUS: rhBMP-2/ACS: Not approved for this indication.

doi: 10.1016/j.spinee.2007.07.395

Wednesday, October 24, 2007
5:25–6:25 PM
Special Interest Poster Presentation 2: Kyphoplasty/Deformity

32. Transforaminal Lumbar Interbody Fusion with Bone Morphogenetic Protein (rhBMP-2) - Risk Factors for Pseudarthrosis

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BACKGROUND CONTEXT: The authors have previously reported vertebral osseous resorption following TLIF with the use of rhBMP-2 in the intervertebral disc space. The effects of osseous resorption, cage surface area, and cage subsidence on lumbar interbody fusion rates has not previously been described. No current study has evaluated risk factors associated with pseudarthrosis.

PURPOSE: To identify whether intervertebral cage surface area, subsidence of the intervertebral cage, osseous resorption, age, or gender affect fusion rates after TLIF with rhBMP-2.

STUDY DESIGN/SETTING: Retrospective computed tomography evaluation to identify risk factors associated with pseudarthrosis after transforaminal interbody fusion augmented with bone morphogenetic protein (rhBMP-2).

PATIENT SAMPLE: Patient sample size was 117.

OUTCOME MEASURES: Thin cut CTs with coronal and sagittal views were used to evaluate fusion.

METHODS: 117 consecutive patients, who had undergone single level TLIF with rhBMP-2 were selected. All patients had rhBMP-2 placed in the interbody space along with an interbody support. Thin cut CT scans with coronal and sagittal reconstructions were performed post-operatively. CT scans were done an average of 6.8 months post-operatively (2.63 to 43.36). An independent radiologist evaluated all CT studies. Cage surface area was categorized in 3 groups (<30%, 30–50%, and >50%). Cage subsidence was defined as Mild <25%, Moderate 25–50%, Severe >50%, or None. Osseous resorption was evaluated and defined in correlation with previous reports.

RESULTS: The patient mean age was 48.5 years. The TLIF levels totaled L1/2 (1), L3/4 (17), L4/5 (64), L5/S1 (35). At final follow-up, 4 of 117 patients (3.4%) had CT confirmation of pseudarthrosis. Cage surface area was <30% (39) levels, 30-50% (64) levels and >50% (14) levels. Cage subsidence was Mild (27) levels, Moderate (8), and Severe (5) levels. Osseous resorption was present in 71 levels. Four levels with pseudarthrosis were present at L1/2 (1) and L4/5 (3). Cage subsidence was noted in all 4 of these levels. Interbody support was <30% in the non-fused levels. Both of these values reached statistical significance when compared with the group mean ($p=0.002$ and $p=0.001$, respectively). The presence of vertebral osseous resorption in all 4 pseudarthrosis was severe (>1x1cm) and did not reach statistical significance, but size of the defect appears to be greater in the non-fusion patients. Although not statistically significant, pseudarthrosis was associated with a higher mean age (56.5 years). There were 69 females and 48 males. Gender did not affect fusion rate ($p=0.277$).

CONCLUSIONS: The TLIF procedure typically employs a small interbody spacer. These results indicate to optimize fusion in patients undergoing TLIF with rhBMP-2 the surgeon should maximize surface area support of the intervertebral cage. Cage subsidence, osseous resorption, and age may be linked to pseudarthrosis. All of these factors should be avoided to promote successful interbody fusion.

FDA DEVICE/DRUG STATUS: rhBMP-2 / Infuse: Not approved for this indication.

doi: 10.1016/j.spinee.2007.07.396

33. Factors Influencing the Results of Surgery for Ossification of the Posterior Longitudinal Ligament in the Thoracic Spine—A Multi-institutional Retrospective Study

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BACKGROUND CONTEXT: Surgical treatment of ossification of the posterior longitudinal ligament in the thoracic spine (T-OPLL) is technically demanding even with recent advance in surgical techniques. Detailed